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Case Report

Surgical treatment for locally advanced pancreatic cancer localized in the pancreatic body and tail (report of 11 cases)

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Abstract: Objective: To investigate the clinical efficacy of radical resection for pancreatic cancer localized in the pancreatic body and tail. Methods: From 2009 to 2013, 11 patients with pancreatic cancer localized in the body and tail were treated with sequential radical resection of the tumor and postoperative chemotherapy, and closely followed up. Results: Among the 11 patients, 7 received R0 resection, 4 received R1 resection. In the rest 2 patients, the tumor was removed together with the involved celiac artery and common hepatic artery. There were no postoperative complications, except second surgery for postoperative ischemic necrosis of the gastric antrum in 1 case, and wound infection in another patient. Nine of the 11 patients underwent cyclic chemotherapy with gemcitabine. Abdominal pain was relieved in all postoperative patients. The postoperative median survival time was 28 months, and 1-year and 3-year survival rates were 81.8% and 36.3%, respectively. Conclusion: Combination of surgical removal of the tumor with adjuvant chemotherapy can achieve better survival and significantly improve the patients' quality of life.

Keywords: Pancreatic cancer, radical resection, chemotherapy

Introduction

Pancreatic cancer is one of the most aggressive malignant tumors, usually manifested upon extensive disease due to its insidious clinical presentations. The current overall 5-year survival rates are less than 5%. The incidence and death rate of this disease is increasing rapidly in China with a trend for younger ages.

About 90% cases of pancreatic cancer are derived from pancreatic duct cells [1]. Anatomically, 60%-80% of pancreatic cancers reside in the pancreas head, and the remaining 25% distribute in pancreatic body or tail. The latter usually lacks of specific early symptoms due to the deep location of the tumor [2]. The common complains of patients with pancreatic cancer in the body or tail are vague upper abdominal pain, upper abdominal discomfort, loss of appetite. The infiltrative growth of the tumor can involve neighboring organs and large blood vessels. Since the disease is usually diagnosed at advanced stage, the patients had been considered inoperable. However, studies show that, among all current available therapy modalities, only surgical intervention can prolong the survival in patients with pancreatic cancer localized in the body or tail of the organ, and radical resection performs better than palliative resection and non-surgical therapies in this sense [3].

The resection rate is currently 10%-30% for pancreatic cancer localized in the body and tail [4]. The patients in advanced stage often suffer from persistent and severe upper abdominal pain and have low life quality. Herein we reported that from 2009, we surgically treated 11 cases, including 10 in stage 3 and 1 in stage 4 (different from the staging on **Table 2**), of patients with pancreatic cancers localized in the body and tail. Radical resection combined adjuvant chemotherapy not only prolonged patients' survival but also markedly improved the patients' quality of life.

Table 1. Clinical data of the patients

#	Age (years)	Tumor localization in the pancreas	Size of tumor (cm)	Invasion of vessel	Metastasis	Operation duration (min)	Intraoperative blood transfusion (ml)
1	49	Body	5.5	CA, SA, SV, LGA	Liver	260	800
2	63	Body & tail	6.0	CA, GDA, SA, SV, LGA	Stomach, duodenum and transverse colon	290	400
3	67	Body & tail	5.5	CA, SA, SV, LGA	Stomach, splenic curvature	345	800
4	59	Body & tail	6.5	CA, SA, SV, LGA	Stomach	270	800
5	78	Body & tail	6.0	SMA, SA, SV, LGA	----	230	400
6	70	Neck and body	6.0	CA,PV, CHA, GDA SA, LGA	----	270	400
7	66	Body & tail	5.5	SMA, SA, SV, LGA	----	320	400
8	55	Body & tail	6.5	SMA, SA, SV, LGA	Stomach	360	400
9	65	Body & tail	5.5	CA, SA, SV	----	330	400
10	57	Body	5.5	CA, SA, SV, LGA	----	360	400
11	52	Body	4.0	CA, SA, SV, LGA	----	340	400

Table 2. Clinical course of the 11 patients

#	Hosptalization time (d)	Postoperative complications	Survival (m)	Abdominal pain after surgery	Pathologic diagnosis	Surgical margin	Stage
1	18	-	9	-	Adenocarcinoma, high grade	R1, resection, positive pancreatic end and lymph nodes	T4N1M1
2	19	-	36	-	Adenocarcinoma, high grade	R0 resection, positive lymph nodes	T4N1M0
3	32	-	36	-	Adenocarcinoma, high grade	R1 resection, positive pancreatic end, surrounding nerves and lymph nodes	T4N1M0
4	29	-	14	-	Adenocarcinoma, intermediate grade, transluminal invasion of stomach	R0 resection, positive lymph nodes	T4N1M0
5	24	-	22	-	Adenocarcinoma, high grade	R0 resection, negative	T4N0M0
6	91	Ischemic necrosis in gastric antrum	22	-	Adenocarcinoma, high grade	R0 resection, positive lymph nodes	T4N1M0
7	14	-	> 44	-	Adenocarcinoma, high grade	R1 resection, positive retroperitoneal margin	T4N0M0
8	29	-	33	-	Adenocarcinoma, high grade	R0 resection, positive lymph nodes	T4N1M0
9	26	-	8	-	Adenocarcinoma, low to intermediate grade	R1 resection, positive pancreatic margin, surrounding nerves and lymph nodes, tumor plug in pancreatic duct	T4N1M0
10	78	Infection in insicion and abdominal cavity	> 38	-	Tubular adenocarcinoma, high grade with focal mucinous feature	R0 resection, positive lymph nodes	T4N1M0
11	14	-	28	-	Adenocarcinoma, high grade	R0 resection, positive lymph nodes	T4N1M0

Figure 1. Invasion of CA and its bifurcation by pancreatic cancer on abdominal enhanced CT.

Materials and methods

Patients

From July 2009 to March 2013, a total of 11 cases of pancreatic cancer localized in the body and tail, 4 females and 7 males, with an average age of 61.9 ± 8.5 years, were admitted to our hospital, a tertiary medical center (**Table 1**). The average tumor size was 5.68 ± 0.68 cm. Among the 11 cases, 10 were stage 3 and 1 stage 4 (2011 National Comprehensive Cancer Network (NCCN)). All the patients were pathologically diagnosed with pancreatic ductal adenocarcinoma.

Preoperative radiological assessment

Preoperative CT, CT angiography and abdominal ultrasonography were used to assess tumor resectability by evaluating involvement of the tumor of adjacent organs, remote organs and the major blood vessels such as celiac artery (CA), common hepatic artery (CHA), superior mesenteric vessels (SMA, SMV), portal vein (PV), proper hepatic artery (PHA), gastroduodenal artery (GDA), splenic artery vessels (SA, SV). The results demonstrated that in 2 of cases, celiac artery and its bifurcation was encased and occluded by the tumor, with GDA also occluded in one of these 2 cases. Involvement of less than one half of circumference of vessel sheath but no stenosis or occlusion of vessel lumen was shown in the rest 9 cases, with involvement of CA in 6 cases and involvement of SMA in 3 cases. Different extent of stenosis/occlusion of SA and SV was observed in all the 11 cases of cancer due to tumor infiltration. Radiology studies also revealed involvement of adjacent organs 4 of the 11 cases, and multiple liver metastases in 1 case (**Table 1**; **Figures 1**, **2**).

Surgical therapy

Through subcostal incision in the left upper abdomen, the pancreas was transected on the right side of portal vein followed by ligation of the splenic vein at its merge into portal vein. Then the tumor was dissected from right to left and removed as en block together with the spleen. Among the 11 cases, CA and CHA were removed for the patient with complete encasement of CA and its bifurcation. The blood supply for this patient's liver and stomach was therefore provided by gastroduodenal artery from the superior mesenteric artery postoperatively. Resection of CA, CHA and GDA was performed for another patient, without concomitant gastrectomy (**Figure 3**).

Invasion of blood vessel sheath by tumor was present in the remaining 9 cases- 6 with involvement of CA and 3 with infiltration of SMA. For these patients, the vessel sheath was opened to facilitate en block of the tumor together with the vessel sheath. Resection LGA, dissection of lymph nodes surrounding CA and removal of retroperitoneal plexus was done on all the patients. Since involvement and occlusion of splenic vessels present on all the cases, the spleen together its vessels was removed.

Intraoperative injection of ethanol to hepatic masses was done under ultrasound guidance for 1 case with 2 liver metastases. For the 3 cases with tumor invasion into posterior stomach wall, local resection or total gastrectomy was carried out depending on the extent of the involvement of stomach by the tumor. In the case with tumor invading posterior wall of the stomach and splenic curvature of the colon, partial resection of the posterior wall of the stomach and resection of splenic curvature of the colon was done. As to the patient with tumor violating the posterior wall of the stomach, duodenum and the transverse colon, the affected parts and the tumor was removed with wide resection. The exposed end of the main pancreatic duct was closed by suturing, except the patient with liver metastasis, in whom pancreatojejunal Roux-en-Y anastomosis was performed to drain the proximal part of the pancreas.

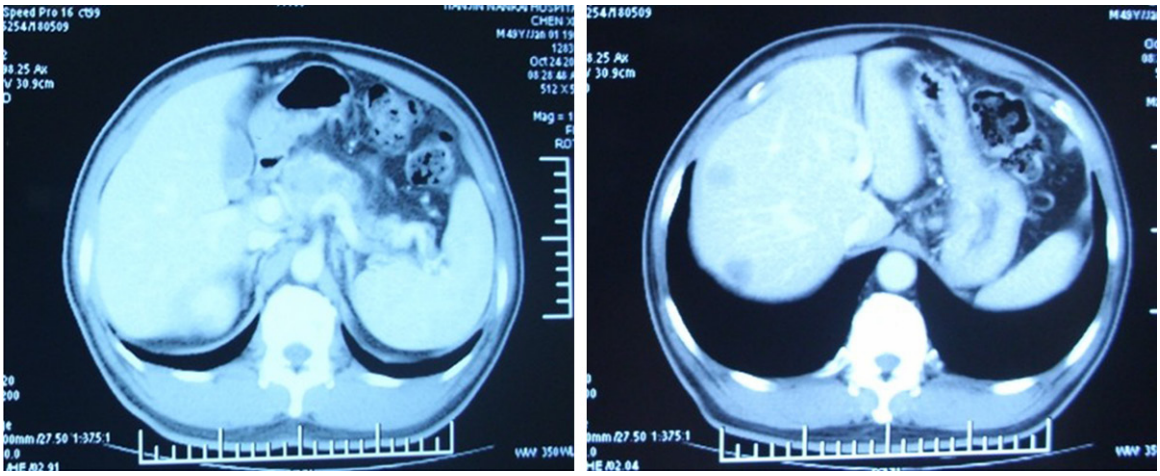

Figure 2. Invasion of CA and its bifurcation by pancreatic cancer, and liver metastases on abdominal enhanced CT.

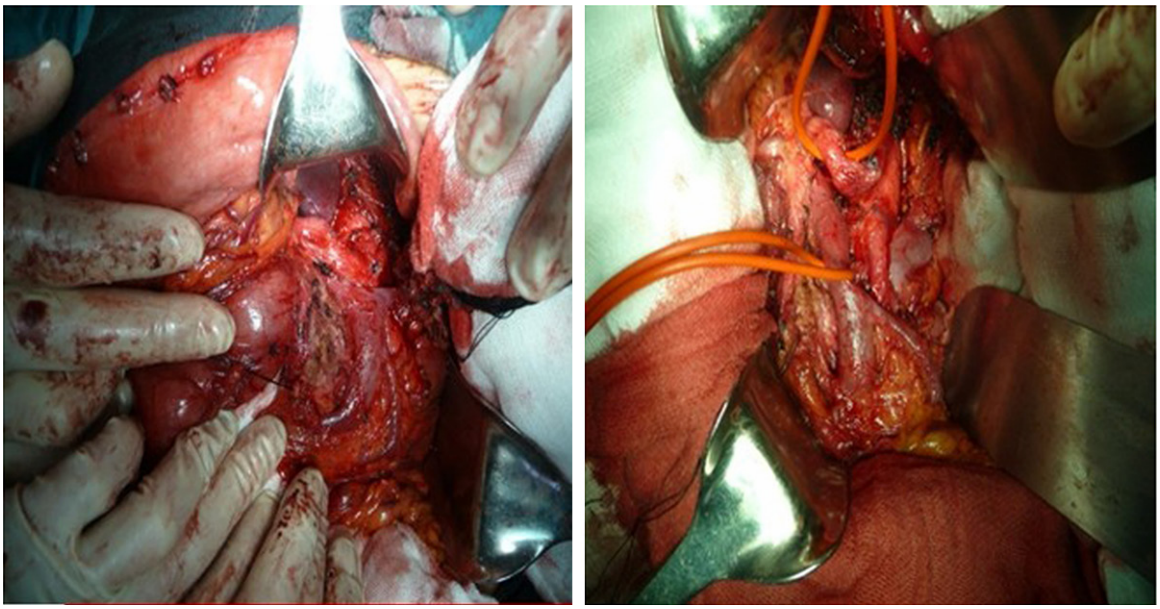

Figure 3. Skeletonized blood vessels after removal of the tumor, and the exposed pancreatic end.

Chemotherapy and follow up

All patients received post-surgery monotherapy with weekly intravenous gemcitabine in 100 ml of saline, 3 weeks in a cycle. Monitoring with CBC and BMP was done before infusion. The patients were followed up with serum CA19-9 and abdominal CT after each cycle.

Results

Seven of the patients received R0 resection and 4 did R1 resection. The 1 year, 2-years and 3-year survival rates of the 11 patients were 81.8%, 54.5%, and 36.3%, respectively. The median survival of the patients was 28 months, with one case of more than 44 months of tumor free survival. The patient with liver metastases survived 9 months postoperatively. R0 resection was still achieved in the patient undergoing a second surgery (gastrectomy). The patient also received chemotherapy for 18 months, survived 22 months without recurrence postoperatively but died of cachexia due to refusal of further therapy (**Table 2**).

The patient with resection of CA, CHA and GDA experienced gastroduodenal fistula on day 14

postoperatively, presenting fever and abdominal pain. Radiology studies revealed the location of fistula. Preoperative CT imaging showed compression by the tumor on celiac artery and portal-splenic confluence. A second surgery was done on day 40 postoperatively upon failure of therapy with drainage and antibiotics. Intraoperative examination demonstrated necrotic perforation in gastric antrum and acute cholecystitis, with involvement of portal vein, GDA, CHA, CA, left gastric artery and splenic artery. Treatment of the patient with gastrectomy, cholecystectomy, gastrojejunal loop anastomosis, resection affected CA, CHA, GDA, left gastric artery and splenic artery, and postoperative support achieved resolve of the fistula, without impairment of liver function. Another patient was complicated with postoperative incision and abdominal infection, which was corrected with antibiotics and support therapy. No complications occurred in the remaining patients. Abdominal pain resolved in all the patients, with no significant impairment of liver function observed in any of them.

Discussion

Despite advances in the multidisciplinary treatment of pancreatic cancer over the last few years, the prognosis is this tumor is still very poor, with one-year survival rate of less than 20% and 5-year survival rate of less than 5% [5]. Low respectability accounts largely for the formidable clinical outcomes. Especially, when the tumor resides in the body and tail of the organ, its deep location and lacking of specific symptoms makes early diagnosis more difficult. Very often, the patients have distant organ metastasis or major blood vessels involvement at diagnosis. The reported 5-year survival rates is 10% in Western countries, but higher in Japan, probably due to implementation of aggressive surgery by Japanese surgeons. In our study, combination of radical surgery and chemotherapy greatly improved the patients' symptoms and prolonged their survival.

Classic surgery procedure for pancreatic cancer in the body and tail consists of removal of spleen with the tumor, and dissection of fat and lymphatic tissue around splenic vessels, abdominal aorta, celiac artery, hepatoduodenal ligament, and common hepatic artery [6]. The determinant factors for success of this manual include abdominal metastasis and invasion of major blood vessels surrounding the tumor, most frequently seen in celiac artery and hepatic artery. Yet the tumor occasionally adheres to confluence of portal vein, stomach and/or transverse colon, and duodenum, which imposes extra difficulty on surgery.

Consensually, the determinator for achieving radical surgical resection in the classic procedure is the extent of tumor invasion of the celiac artery, namely whether the tumor can be completely removed from the involvement of the CA. People believe that when celiac artery and its bifurcation involved, the tumor is unresectable because blood supple for the liver and stomach from celiac artery and common hepatic artery cannot be interrupted. However, studies have shown that this restriction can be nonsignificant due to preexisting variant hepatic artery and formation of collateral circulation triggered by the preoperative, gradual occlusive vascular involvement by the tumor. Thus, most often, the liver and stomach has tolerated the aberrant blood supply before surgery. On the other hand, some surgeons believe that respectability of the tumor depends on extent of involvement of the SMA. In fact, 60% of the preoperative radiological findings of vascular involvement in pancreatic cancer turned out to mass effect or chronic peri-pancreas inflammation on pathological examination [7]. Therefore, we believe that involvement of the celiac artery and its branches should not be a contraindication to resection. To ensure negative surgical margins, extended radical resection can be considered under circumstance of vessel-infiltrated pancreatic cancer [8]. In Shoup's series, the 5 and 10 year survival following the surgery is 22% and 18%, respectively [9]. In the present study, resection of the sheath of CA and CHA/GDA or the vessels was performed in all 11 cases, which not only facilitated radical resection of the tumor but resulted in improved survival for the patients. It is noteworthy to point out that resection of these vessels should be accompanied with cholecystectomy and gastrectomy, because the stomach and gallbladder lose their major blood supply. This is true with one of our cases in whom ischemic necrotic perforation occurred in gastric antrum post the surgery, due to absence of adequate perfusion from either variant or collateral blood vessels entering the stomach.

The 2 cases receiving R1 resection in the present study had relative long survival of 36 and more than 44 months, respectively. Although the surgery is less extensive in these 2 patients comparing that in the cases with R0 resection, gemcitabine therapy might play an important role in their clinical outcome. But it is not clear so far if surgery can improve the patient's survival in those with distant metastasis. To answer this question, we need more prospective clinical data.

In summary, we believe that radical resection can be selected for the patients with pancreatic cancer localized in pancreatic body and tail but without distant metastasis. Combinatorial adjuvant gemcitabine chemotherapy should be implemented for better clinical outcomes. We also believe that early diagnosis of this disease is also a necessary means to improve the prognosis.

Disclosure of conflict of interest

None.

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References

[1] Cubilla AL and Fitzgerald PJ. Morphological lesions associated with human primary invasive nonendocrine pancreas cancer. Cancer Res 1976; 36: 2690-8.

[2] Matsuno S, Egawa S, Fukuyama S, Motoi F, Sunamura M, Isaji S, Imaizumi T, Okada S, Kato H, Suda K, Nakao A, Hiraoka T, Hosotani R, Takeda K. Pancreatic Cancer Registry in Japan: 20 years of experience. Pancreas 2004; 28: 219-30.

[3] Yekebas EF, Bogoevski D, Cataldegirmen G, Kunze C, Marx A, Vashist YK, Schurr PG, Liebl L, Thieltges S, Gawad KA, Schneider C, Izbicki JR. En bloc vascular resection for locally advanced pancreatic malignancies infiltrating major blood vessels: perioperative outcome and long-term survival in 136 patients. Ann Surg 2008; 247: 300-9.

[4] Saisho H and Yamaguchi T, Diagnostic imaging for pancreatic cancer: computed tomography, magnetic resonance imaging, and positron emission tomography. Pancreas 2004; 28: 273-8.

[5] Wood HE, Gupta S, Kang JY, Quinn MJ, Maxwell JD, Mudan S, Majeed A. Pancreatic cancer in England and Wales 1975-2000: patterns and trends in incidence, survival and mortality. Aliment Pharmacol Ther 2006; 23: 1205-14.

[6] Chauffert B, Mornex F, Bonnetain F, Rougier P, Mariette C, Bouché O, Bosset JF, Aparicio T, Mineur L, Azzedine A, Hammel P, Butel J, Stremsdoerfer N, Maingon P, Bedenne L. Phase III trial comparing intensive induction chemoradiotherapy (60 Gy, infusional 5-FU and intermittent cisplatin) followed by maintenance gemcitabine with gemcitabine alone for locally advanced unresectable pancreatic cancer. Definitive results of the 2000-01 FFCD/SFRO study. Ann Oncol 2008; 19: 1592-9.

[7] Peng C. Attaches great importance to preoperative pancreatic cancer surgery resectable evaluation. Journal of Surgery Concepts Practice 2007; 12: 3.

[8] Yamada S. Pancreatic cancer with paraaortic lymph node metastasis: a contraindication for radical surgery? Pancreas 2009; 38: e13-7.

[9] Shoup M, Brennan MF, McWhite K, Leung DH, Klimstra D, Conlon KC. The value of splenic preservation with distal pancreatectomy. Arch Surg 2002; 137: 164-8.